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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,468	07/10/2003	Patrick M. Hughes	17549 (AP)	3251

7590 01/30/2009

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EXAMINER	
BETTON, TIMOTHY E	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
01/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/617,468	HUGHES ET AL.	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *5,18 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date : 10/9/2007 and 2/24/2005, 2 sheets, respectively.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10617468	7/10/2003	HUGHES ET AL.	17549 (AP)

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EXAMINER
TIMOTHY E. BETTON

ART UNIT	PAPER
1617	20080408

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

Applicants election filed 16 January 2008 has not been found responsive to the species election requirement. Applicants were required to specifically elect species from instant claims 3-7, 9, 13, and 15 as disclosed in the action filed 31 December 2007. However, applicants have only elected carboxylic acid and claims 1-17 and 19 which does not sufficiently or adequately meet the required election of species as disclosed in the said action 31 December 2007.

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DETAILED ACTION

Applicant's election without traverse of additional requirement of an election of species in the reply filed on 18 June 2008 is acknowledged.

Applicants hereby identify tazarotene as the prodrug and tazarotenic acid as the drug. Tazarotene is an ester of tazarotenic acid. Both compounds are retinoids and are sulfur- based. (See formula 1 on page 11 of the present specification.) Therefore, claims 3, 4 and 6-9 read on this species. (It is not understood why the Examiner is not including claim 8 in his action, since tazarotene in claim 8 is the prodrug of tazarotenic acid, which is the active drug of claim 7.)

Claims 5, 18, and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 18 June 2008.

Applicants' Remarks filed 9 October 2007 are acknowledged and duly made of record.

Accordingly, in consideration of applicants' response to the 112 1st paragraph rejection, the rejection is hereby withdrawn.

Any other rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application, i.e., the previous 103(a) rejection is being maintained.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 , 6-17, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campochiaro et al (USPN 6, 071,924), Allergan [online] Tazarotene Proliferative Vitreal Retinopathy, retrieved December 18, 2007, (2001), retrieved from http://www.shareholder.com/AGN/downloads/2001AnnualReport.pdf., (especially page 14), Wilkin ,J. (Allergan, Inc. Avage (tazarotene) cream, 0.1% Irvine California 92612, USA (2002), printed pages 1-17, especially page 1), and Castelhano et al. (USPGPUB 2003/0073708 A1) in view of Yewey et al. (USPN 5,780,044) and Chang (USPN 5,275,820).

Campochiaro et al. teach a mode of retinoid delivery (c. 3, l. 16)

Campochiaro et al. teach intravitreally or **subconjunctival** injection of [a] retinoid (c.5, l. 28).

Campochiaro et al. does not teach tazarotene expressly.

Allergan reports the ophthalmic pharmaceutical Oculex in 2001 which is the trade/brand for Tazarotene. According to the report, Tazarotene is specifically indicated for vitreal retinopathy (page 14).

Allergan does not disclose that the active drug is an alcohol or a prodrug as an ester of a phosphorus or sulfur-based acid.

However, Wilkin does disclose an embodiment directed to the pharmacokinetics of tazarotenic acid. With the exception of the indication as a topical cream, the skilled artisan would

instantly recognize the active drug, tazarotenic acid would still maintain inherent properties, characteristics and susceptibilities.

Following topical application, tazarotene undergoes esterase hydrolysis to form its active metabolite tazarotenic acid. Little parent compound could be detected in the plasma. Tazarotenic acid was highly bound to plasma proteins (>99%). Tazarotene and tazarotenic acid were metabolized to sulfoxides, sulfones, and other polar metabolites which were eliminated through urinary and fecal pathways (last paragraph, page 1).

Castelhano et al. teach an embodiment directed to a periocular injection formulation of a use of prodrugs which are converted in vivo to therapeutic compounds via esterification [paragraph 0023; 0084; 0092; 0124].

The invention further contemplates the use of prodrugs which are converted in vivo to the therapeutic compounds of the invention. Such prodrugs can be used to alter the biodistribution (e.g., to allow compounds which would not typically enter the reactive site of the protease) or the pharmacokinetics of the therapeutic compound. For example, a carboxylic acid group, can be esterified, e.g., with a methyl group or an ethyl group to yield an ester. When the ester is administered to a subject, the ester is cleaved, enzymatically or non-enzymatically, reductively or hydrolytically, to reveal the anionic group. An anionic group can be esterified with moieties (e.g., acyloxymethyl esters) which are cleaved to reveal an intermediate compound which subsequently decomposes to yield the active compound. In another embodiment, the prodrug is a reduced form of a sulfate or sulfonate, e.g., a thiol, which is oxidized in vivo to the therapeutic compound. Furthermore, an anionic moiety can be esterified to a group which is actively transported in vivo, or which is selectively taken up by target organs. The ester can be selected to

allow specific targeting of the therapeutic moieties to particular reactive sites, as described below for carrier moieties (paragraph 159).

With the exception of instant claims 9 and 14, Castelhano, however, does not teach a microparticle system and/or a microsphere suspension.

Yewey et al. resolves the deficiency in Castelhano by teaching an [i]mproved biocompatible liquid delivery compositions, which are useful for the formation of sustained release delivery systems for active agents, are provided. The compositions include liquid formulations of a biocompatible polymer or prepolymer in combination with a controlled release component. The controlled release component includes an active agent. These compositions may be introduced into the body of a subject in liquid form which then solidify or cure in situ to form a controlled release implant or a film dressing. The liquid delivery compositions may also be employed ex situ to produce a controlled release implant. Methods of forming a controlled release implant and employing the liquid formulations in the treatment of a subject are also provided (abstract only).

Yewey et al. teach a number of conventional controlled release systems are based on microstructures, such as lipospheres, liposomes, microcapsules, **microparticles**, and nanoparticles (col. 1, l/s 15-17).

Yewey et al. teach [a] **polymeric system** [which] includes reactive liquid oligomeric prepolymers which cure by cross linking to form solids, usually with the aid of a curing agent (col. 2, l. 8)

Yewey et al. teach that the monomer ratios (D,L-lactide versus malolactonic acid) may be varied to obtain the balance of water insolubility and carboxyl group content desired for a

particular application. In some instances, in order to obtain a copolymer with the properties desired, it may be advantageous to use other combinations of monomers. **For example, MLABE may also be polymerized with glycolide** or caprolactone to yield, after removal of the benzyl protecting groups by hydrogenation, poly(glycolide-co-malolactonic acid) or poly(caprolactone-co-malolactonic acid) respectively. Terpolymers such as **poly(D,L-lactide/glycolide** /malolactonic acid) may also be prepared by the same method (col. 15, l. 11).

Chang adequately addresses the deficiency in Castelhano et al. by teaching sustained release pharmaceutical compound delivery compositions and methods for their production [which] are disclosed wherein ion exchange resin particles are loaded with releasably bound pharmaceutical compounds prior to incorporation in an erodible polymeric matrix to form microparticulates. The microparticulates are suspended in a fluid medium where the encapsulating polymeric matrix shields the drug loaded ion exchange resin from solvent interaction. Administration to target tissue site initiations erosion of the polymer matrix and release of the loaded pharmaceutical compound (abstract only).

Further, Chang teaches methods of retaining effective quantities of these compounds in contact with targeted tissue sites or areas for sufficient periods of time to accomplish the desired therapeutic or diagnostic effect (column 1, lines 24-28).

Thus, it would have been prima facie obvious to the skilled artisan at the time of invention to at once incorporate and/or combine together the teachings and methods of Campochiaro et al., Allergan, Wilkins, Castelhano et al. and Chang.

Campochiaro et al. essentially encompasses the inventive objective of the current claimed invention. The elected agent which is a retinoid has been taught in prior art as indicated for other modes of administration including subconjunctivally.

Accordingly in view of obviousness over claimed invention, Allergan discloses the direct indication for tazarotene as an eye composition for use in vitreal retinopathy. Wilkin discloses package insert information in relation to the prodrug/ active metabolite of tazarotenic acid and the esterification process via a sulfur-based acid. Accordingly, it is well-established in the art that tazarotenic acid does not meet the classification requirements as a platelet activating factor antagonist. Castelhano et al. adequately encompasses subject matter of claimed invention with the exception of the particular dosage formulation. The skilled artisan would instantly see the motivation in to combine the Castelhano reference with the teachings of Yewey et al. based on the shared subject matter by Chang. Yewey et al. teaches the specific limitation drawn to a particular polymeric system as disclosed above. Chang, also in addition discloses methods and teachings drawn to the administration of active agents via microparticles and formulates associated. Chang supports and suggests the inventive objective of instant claims by teaching subject matter directed to a sustainable therapeutic administration to targeted tissue sites. Thus, there would be the motivation to incorporate together and combine the references based on Allergan reporting tazarotene as an eye composition for use in vitreal retinopathy, which would be administration to a targeted tissue site.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shengjun Wang/

Primary Examiner, Art Unit 1617

TEB